DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2004D–0493]

1-3-06
1-4-06

Guidance for Industry and Review Staff on Recommended Approaches to Integration of Genetic Toxicology Study Results; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry and review staff entitled "Recommended Approaches to Integration of Genetic Toxicology Study Results." This guidance is intended to inform industry and the review staff in the Center for Drug Evaluation and Research (CDER) on how CDER views positive findings in genetic toxicology assays during drug development. The guidance provides recommendations on how to proceed with clinical studies while ensuring the safety of study participants when results in genotoxicity studies suggest a potential cancer or genetic hazard.

DATES: Submit written or electronic comments on agency guidances at any time.

ADDRESSES: Submit written requests for single copies of this guidance to the Division of Drug Information (HFD–240), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Send one self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the guidance to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers

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Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.fda.gov/dockets/ecomments*. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: David Jacobson-Kram, Center for Drug Evaluation and Research (6411), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 6488, Silver Spring, MD 20993, 301–796–0175.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry and review staff entitled "Recommended Approaches to Integration of Genetic Toxicology Study Results." Pharmaceuticals administered through oral, intravenous, topical, and other routes, as appropriate, are subject to this guidance.

In the **Federal Register** of December 2, 2004 (69 FR 70153), FDA announced the availability of a draft version of the guidance entitled "Recommended Approaches to Integration of Genetic Toxicology Study Results." When the draft guidance was published, FDA requested comments on the document. Some changes were made to the draft document based on comments submitted to the docket including the following changes: (1) The guidance now suggests that for a compound giving positive results in a genetic toxicology assay, an alternative to demonstrating "mechanism of action" would be ruling out mechanisms involving direct interaction with dexoyribonucleic acid (DNA) and (2) alkaline elution is included as an example of an assay for measuring DNA damage. Other editorial changes were also made.

A number of comments to the docket suggested that the fourth test in the International Conference on Harmonisation (ICH) battery should be an option for compounds giving a positive response in one of the initial assays. This

change was not included. Positive responses are primarily seen in the in vitro chromosomal aberration assay and/or the mouse lymphoma assay. Because these two tests measure common genetic lesions and have similar drug exposure protocols, the data from the two assays can be used to corroborate results.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the agency's current thinking on recommended approaches to integration of genetic toxicology study results. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

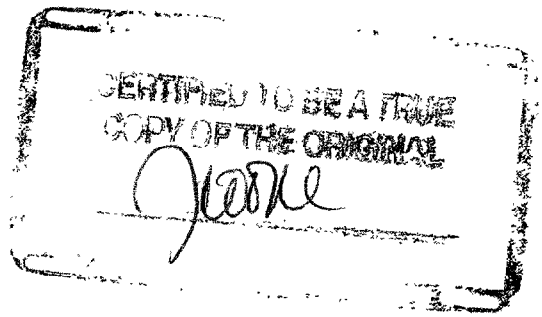
II. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments on the guidance at any time. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The guidance and received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

III. Electronic Access

Persons with access to the Internet may obtain the document at either *http://www.fda.gov/cder/guidance/index.htm* or *http://www.fda.gov/ohrms/dockets/default.htm.*

Dated: 12/21/05
December 21, 2005.



Jeffrey Shuren,
Assistant Commissioner for Policy.

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